REMARKS

Claims 1-3, 7 and 8 are pending in this application. Claims 7 and 8 have been allowed. Claims 1-3 have been rejected. Claims 1 and 2 have been amended. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Claim rejections under 35 USC §112

Claims 1-3 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, claims 1 and 2 recite the term "spleen-derived", wherein the metes and bounds of what is meant by derived is suggested as being indefinite because how similar or different from any other cell obtained by a different means or source is not clearly set forth in the claim nor the specification. Applicants respectfully disagree. Applicants describe a population of myeloid-committed stem cells obtained from spleen which are depleted of T-cells, stimulated with LPS, transduced and used in the treatment of lysosomal storage diseases. See page 13 (lines 30-33) and Example II. Thus, in an earnest effort to facilitate the prosecution of the instant application, Applicants have amended claims 1 and 2 to indicate that the myeloid-committed stem cells are obtained from spleen. Support for this amendment is found in claim 7, step a), which recites that myeloid-committed stem cells of the invention are obtained from spleen. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claims 1 and 2 (and dependent claim 3) have been rejected under 35 U.S.C. 112, first paragraph as containing subject matter which was not described in the specification ins such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time of filing, had possession of the claimed invention. The Examiner acknowledges that the specification supports the fact that stem cells can be obtained from the spleen, however, the term "spleen-derived" has no literal support. Further, it is suggested that the specification fails to provide the necessary description of such a cell that would allow the artisan to clearly establish the claimed cell from other cells obtained from other tissue sources by other means.

Claims 1-3 have also been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner suggests that the specification provides for the isolation of a pluripotent cell from the spleen, however, fails to provide other methodology or a detailed characterization of the claimed cell. Applicants respectfully disagree with these rejections.

As indicated above, Applicants have identified a unique population of cells obtained from the spleen. Examples I and II of the specification provide the necessary methodology for obtaining this population of cells, *i.e.*, generating a single cell suspension from spleen tissue and depleting the suspension of T-cells. Accordingly, the claimed composition of cells can be distinguished from other cells based upon being obtained from the spleen and

being deficient of T-cells. Moreover, Applicants have appreciated that upon LPS stimulation (*i.e.*, lipopolysaccharides), these cells are readily transduced and used for treatment of diseases. In particular, page 16 (lines 6-10) states

> "LPS-stimulated, T cell-depleted spleen cells were infected with retroviral vector containing the neomycin phosphotransferase (neo) marker gene and were used to rescue lethally-irradiated syngeneic recipients."

Thus, in an earnest effort to clarify the phenotypic characteristics of the claimed compositions, Applicants have amended the claims to indicate that cells of the composition are lipopolysaccharide-stimulated, transduced, obtained from spleen, and deficient of T cells. Support for this amendment can be found at page 6 (lines 6-10) and Example I (the paragraph bridging pages 20 and 21), in view of Ulevitch and Tobias ((1995) *Annu. Rev. Immunol.*13:437-57; abstract enclosed herewith) who teach that lipopolysaccharide, also known as LPS, is a stimulant for myeloid and nonmyeloid lineage cell activation. In making these amendments, Applicants have provided a source of the claimed cells (*i.e.*, spleen) and measurable phenotypic characteristics which facilitate transduction of the stem cells and are useful for distinguishing this population of cells from other populations of cells (*i.e.*, lipopolysaccharide-stimulated and deficient of T cells). These characteristics are readily determined by the skilled artisan using established methods and methods disclosed in the instant application. For example, Ulevitch and Tobias teach that it LPS is known to trigger induction of cytokines, adhesive proteins, and

enzymes by myeloid lineage cells; phenotypes measurable by standard northern or western blot analyses. The sentence bridging pages 20 and 21 of the instant specification also teaches that LPS-stimulation facilitates gene transduction; a response measurable by transducing the claimed population of cells and identifying the exogenous nucleic acids in the cells (see Figure 5 and page 26, lines 28-31). Moreover, the paragraph bridging pages 17 and 18 of the specification teaches that stem cells obtained from spleen are depleted of T-cells using an anti-Thy-1.2 antibody and complement; a feature which facilitates the transduction efficiency of the stem cells (see the sentence bridging pages 20 and 21). Accordingly, the skilled artisan would readily appreciate that a myeloid-committed stem cell population deficient of T-cells would lack expression of art-established T-cell-specific surface markers such as Thy-1.2.

Because the claim amendments provide a more specific description of the instant transduced, myeloid-committed stem cells obtained from spleen, Applicants respectfully believe that a new search of the art is not required as the scope of the claims has not been broadened by these amendments. In light of these amendments, Applicants believe that written description and enablement requirements have been met and therefore respectfully request reconsideration and withdrawal of rejections under 35 U.S.C. 112, first paragraph.

II. Claim rejections under 35 USC §102

Claims 1-3 remain rejected under 35 U.S.C. 102(b) as being anticipated by Freas-Lutz et al. ((1994) *Exp. Hematol.* 22:857-65).

Claims 1 and 2 also remain rejected under 35 U.S.C. 102(b) as being anticipated by Migita et al. ((1995) *Proc. Natl. Acad. Sci. USA* 92:12075-12079). The Examiner suggests that nothing in the claims nor the specification provides for more than a functional limitation that the myeloid-committed stem cell is capable of differentiating into myeloid lineages and that the M1 cells of Freas-Lutz et al. and the CD34+ cells of Migita et al. meet this functional requirement. It is suggested that Freas-Lutz et al. teach various retroviral constructs using various promoters to analyze expression and activity of glucocerebrosidase and include the use of phosphoglycerate gene promoter which is expressed in macrophages, a differentiated myeloid cell. It is further suggested the Migita et al. likewise teach the use of retroviral vectors for transfection and expression of an exogenous nucleic acid sequence encoding glucocerebrosidase. It is suggested that because the instant specification does not specifically define what a myeloid-committed stem cell is, the broadest interpretation is that the cell is any cell with a restricted ability to become a differentiated cell of the myeloid lineage, and the M1 and CD34+ cells of Freas-Lutz et al. and Migita et al., respectively, meet this interpretation. Applicants respectfully disagree.

Freas-Lutz et al. teach a bone marrow-derived cell line isolated from a SJ mouse with spontaneous myeloid leukemia and transduction with retroviral vectors. See abstract. Similarly, Migita et al. teach viral transduction of CD34+ cells in the presence of protamine sulfate, IL-3, IL-6 and stem cell factor. See page 12076, column 1 under heading "Tranduction of Target Cells." In contrast, the instant myeloid-committed stem cells are obtained

from spleen, are T-cell deficient, lipopolysaccharide-stimulated and transduced; phenotypes which are not characteristic in the cells of Freas-Lutz et al. and Migita et al. Because Freas-Lutz et al. and Migita et al. fail to teach or suggest all of these essential features of myeloid-committed stem cells of the invention, these references fail to anticipate the same. It is therefore respectfully requested that these rejections be withdrawn.

III. Allowable Subject Matter

Applicants acknowledge the allowance of claims 7 and 8. However, because Applicants believe that the proposed claim amendments overcome the rejection of claims 1-3 under 35 U.S.C. §102 and §112, Applicants respectfully request reconsideration of claims 1-3 and allowance of all pending claims as presented herein.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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Date: **November 29, 2005**

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